

SUMMARY OF SAFETY AND EFFECTIVENESS

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Summary of Safety and Effectiveness

General Information	Device Generic Name	Intravascular Stent with Delivery System
	Device Trade Name:	TAXUS TM Express ^{2TM} Paclitaxel-Eluting Coronary Stent System (Monorail) TAXUS TM Express ^{2TM} Paclitaxel-Eluting Coronary Stent System (Over-the-Wire)
	Applicants name and address	Boston Scientific Corporation One Boston Scientific Place Natick, MA 01760
	PMA Number	TBD
	Date of Panel Recommendations	TBD

Device Description

The Boston Scientific TAXUS Express² Coronary Stent System consists of a Paclitaxel eluting balloon expandable stent, pre-mounted on a high-pressure delivery catheter used in the treatment of coronary artery disease. The TAXUS Express² Paclitaxel-Eluting Coronary Stent Systems are represented by two delivery catheters: Express² Monorail and Express² Over The Wire Stent Delivery Systems. The characteristics of the TAXUS Express² stent and delivery system are described in **Table 1**.

Table 1 Device Component Description		
	TAXUSTM Express^{2TM} Stent Monorail Stent Delivery System	TAXUSTM Express^{2TM} Stent Over-The-Wire Stent Delivery System
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32	8, 12, 16, 20, 24, 28, 32
Available Stent Diameters (mm)	2.50, 2.75, 3.00, 3.50	2.50, 2.75, 3.00, 3.50
Stent Material	A 316L surgical grade stainless steel Express stent with a conformal coating of a polymer carrier loaded with 1 µg/mm ² paclitaxel in a slow release formulation with a maximum nominal drug content of 209 µg on the largest stent (3.50x32mm).	
Delivery System Working Length	140 cm	135 cm
Delivery System Y-Adapter Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 25 cm from tip. Designed for guidewire ≤ 0.014"	Y-Connector (Side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire ≤ 0.014"
Stent Delivery Balloon	A balloon enabling high pressure inflations that can be used for post stent dilatation. Two radiopaque markers which aid in the accurate placement of the stent.	
Balloon Inflation Pressure	Nominal Inflation Pressure: 9 ATM; Rated Burst Inflation Pressure: 18 ATM	
Guide Catheter Inner Diameter	≥ 0.058"	≥ 0.066"
Catheter Shaft Outer Diameter	All model sizes are 1.8F proximally and 2.7F distally, with the exception of the 3.50mm in 24, 28, 32 lengths, which are 2.0F proximally and 2.7F distally.	3.2F proximally, 2.7F distally

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Indications for Use

The TAXUS Express² Paclitaxel-Eluting Coronary Stent System is indicated for improving luminal diameter and reducing restenosis for the treatment of *de novo* lesions ≤ 28 mm in length in native coronary arteries ≥ 2.5 to ≤ 3.75 mm in diameter.

In a pivotal US trial, the TAXUS Express² Paclitaxel-Eluting Coronary Stent System has been shown to improve patient outcomes at 9 months when compared to uncoated (bare metal) stents. Specifically, the TAXUS Express² Stent has proven to significantly reduce restenosis, Target Lesion Revascularization (TLR), Target Vessel Revascularization (TVR) and late loss while allowing for sufficient tissue growth over struts of the stent.

Long-term outcomes in large, randomized, multi-center, controlled trials (beyond 12 months) for this implant are unknown at present.

Contra-indications

The TAXUS Express² Paclitaxel-Eluting Coronary Stent System is contraindicated in patients with:

- Known hypersensitivity to paclitaxel or its derivatives
- Patients in whom anti-platelet and/or anticoagulant therapy is contraindicated.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.
- Known allergy to stainless steel.

Warnings

- To maintain sterility, the inner package should not be opened or damaged prior to use.
 - The use of this device carries the risks associated with coronary artery stenting, including subacute thrombosis, vascular complications, and/or bleeding events.
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Summary of Safety and Effectiveness

Precautions

1. General Precautions

- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent stent blockage may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is not well characterized.
- Do not use in patients with history of severe reaction to contrast agents that cannot be adequately premedicated prior to the procedure.
- Do not expose the delivery system to organic solvents, such as alcohol, or detergents.
- Antiplatelet therapy is recommended for a period of 6 months post procedure.

2. Use of Multiple Stents

The extent of the patient's exposure to drug and polymer is directly related to the number of stents implanted. Use of more than two TAXUS Express² Stents has not been fully evaluated. When multiple stents are required, resulting in stent to-stent contact, stent materials should be of similar composition to avoid the possibility of dissimilar metal corrosion.

3. Brachytherapy

The safety and effectiveness of the TAXUS Express² Stent in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of use of brachytherapy to treat in-stent restenosis in a TAXUS Express² Stent has not been established.

4. Use in Special Population

- **Pregnancy:** There are no adequate and well controlled studies in pregnant women or men intending to father children. Systemic levels of paclitaxel have not been demonstrated in any pre-clinical or clinical trials with the TAXUS Express² Stent.
 - **Pediatric use:** The safety and efficacy of the TAXUS Express² Stent in pediatric patients have not been established.
 - **Geriatric Use:** Clinical studies of the TAXUS Express² Stent did not find that patients age 65 years and over differed with regard to safety and efficacy compared to younger patients.
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Summary of Safety and Effectiveness

Precautions Continued

5. Lesion/Vessel Characteristics

The safety and effectiveness of the TAXUS Express² Paclitaxel-Eluting Coronary Stent System have not been established in the following patient populations:

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters < 2.5 mm or > 3.75 mm.
- Patients with lesions located in the left main coronary artery, ostial lesions, or lesions located at a bifurcation.
- Patients with diffuse disease or poor overflow distal to the identified lesions.
- Patients with tortuous vessels in the region of the obstruction or proximal to the lesion.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.

6. Drug Interaction

Because systemic levels of paclitaxel have not been detected post-stent placement in clinical trials, possible interactions of paclitaxel with concomitantly administered medications have not been formally investigated. Drug interactions of systemic chemotherapeutic levels of paclitaxel with possible concomitant medications are outlined in the labeling for finished pharmaceuticals containing paclitaxel, such as Taxol®. Given that the amount of paclitaxel loaded onto each TAXUS Express² Stent is at a minimum 1000 times lower than that used in oncological applications of the drug and is released at considerably lower levels than this, drug interactions are unlikely to be detectable.

7. Magnetic Resonance Imaging (MRI)

Do not perform Magnetic Resonance Imaging (MRI) scan on patient's post-stent implantation until the stent has been completely endothelialized (30 days) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

Summary of Safety and Effectiveness

Precautions Continued

8. Stent Handling

- Note product "Use By" date.
- The TAXUS Express² Stent is designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not designed to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery device. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guiding catheter hub.
- Excessive manipulation, e.g., rolling the mounted stent, may cause coating damage or dislodgment of the stent from the delivery balloon.
- In the event the TAXUS Express² Stent is not deployed, follow product returns procedures and avoid handling of the stent with bare hands.
- Use only the appropriate balloon inflation media. Do not use air or any gas medium to inflate the balloon.
- Stent contact with any fluid prior to placement is not recommended as there is a possibility of drug release. However, if it is absolutely necessary to flush the stent with sterile/isotonic saline, contact time should be limited (1 minute maximum).

9. Stent Placement

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use balloon purging technique described in the Operator's Instructions.
 - Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g., CABG, further dilation, placement of additional stents, or other).
 - When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the more proximal lesion(s). Stenting in this order alleviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.
 - Do not expand the stent if it is not properly positioned in the vessel. (See 10. Stent System Removal – Precautions)
 - Placement of the stent has the potential to compromise side branch patency.
-

Summary of Safety and Effectiveness

Precautions Continued

9. Stent Placement, continued

- The vessel should be pre-dilated with an appropriate sized balloon.
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label. Use of pressures higher than specified on product label may result in a ruptured balloon and potential intimal damage and dissection. The stent I.D. should approximate 1.1 times the reference diameter of the vessel.
- If unusual resistance is felt at any time during lesion access before stent implantation, the Stent System and the guiding catheter should be removed as a single unit. (See 10. Stent System Removal-Precautions.)
- Do not attempt to pull an unexpanded stent back into the guiding catheter while engaged in the coronary arteries, as stent damage or stent dislodgment from the balloon may occur. (See 10. Stent System Removal-Precautions.)
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be subsequently moved in and out through the distal end of the guiding catheter as stent damage or stent dislodgment from the balloon may occur.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the vascular site. Complications can include bleeding, hematoma or pseudoaneurysm.

10. Stent System Removal

- If unusual resistance is felt at any time during lesion access before stent implantation, the Stent System and the guiding catheter should be removed as a single unit.
- Do not attempt to pull an unexpanded stent back into the guiding catheter while engaged in the coronary arteries, as stent damage or stent dislodgment from the balloon may occur.

When removing the entire Stent System and guiding catheter as a single unit (NOTE: The following steps should be executed under direct visualization using fluoroscopy).

Summary of Safety and Effectiveness

Precautions Continued

10. Stent System Removal, continued

- Maintain guidewire placement across the lesion during the entire removal process. Carefully pull back the Stent System until the proximal balloon marker of the Stent System is aligned with the distal tip of the guiding catheter.
- The Stent System and the guiding catheter should be pulled back until the tip of the guiding catheter is just distal to the arterial sheath, allowing the guiding catheter to straighten. Carefully retract the Stent System into the guiding catheter and remove the Stent System and the guiding catheter from the patient as a single unit while leaving the guidewire across the lesion.

Failure to follow these steps, and/or applying excessive force to the Stent System can potentially result in stent damage, stent dislodgment from the balloon and/or damage to the Delivery System.

11. Post Implant

- Care must be exercised when crossing a newly deployed stent with an intravascular ultrasound (IVUS), a coronary guidewire, or a balloon catheter to avoid disrupting the stent placement, apposition, geometry, and/or coating.
- Do not perform Magnetic Resonance Imaging (MRI) scan on patient's post-stent implantation until the stent has been completely endothelialized (30 days) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.
- Prescribe an antiplatelet therapy (i.e. clopidigril or ticlopidine) for a period of 6 months to reduce the risk of stent thrombosis.

Alternative Practices and Procedures

Treatment of patients with coronary artery disease including in-stent restenosis may include exercise, diet, drug therapy, percutaneous coronary interventions (including drug eluting stents) and coronary artery bypass surgery.

Summary of Safety and Effectiveness

Marketing History

The TAXUS Express² Paclitaxel-Eluting Coronary Stent System is commercially available in the following countries listed in **Table 2**.

As of June 1, 2003, approximately 13,000 TAXUS Express² products have been distributed outside of the U.S. No products have been withdrawn from the market in any country for any reason.

Table 2			
Countries Where TAXUS Express² is Commercially Available			
Argentina	Finland	Jordan	Portugal
Austria	France	Liechtenstein	Singapore
Belgium	Germany	Luxemburg	South Africa
Brazil	Greece	Malaysia	Spain
Chile	Hong Kong	Mexico	Sweden
China	Hungary	Netherlands	Switzerland
Columbia	Iceland	Norway	Thailand
Czech Rep.	India	New Zealand	United Kingdom
Denmark	Ireland	Philippines	Uruguay
Egypt	Italy	Poland	

Potential Adverse Events

A total of 1326 patients at 80 sites were enrolled in a pivotal multi-center, randomized, controlled clinical trial (TAXUS IV) to evaluate safety and efficacy of the TAXUS Express stent in a 1 µg/mm² slow release formulation for the treatment of de novo coronary lesions as compared to the bare metal Express control stent.

Additional data is provided for 266 patients enrolled in the slow release formulation arm (Cohort I) of the TAXUS II trial (International Efficacy Study). The TAXUS II study was a multi-center, randomized, controlled trial. Data from 61 patients enrolled in the multi-center, randomized, controlled TAXUS I trial (Randomized Feasibility) are also provided.

The Major Adverse Clinical Events (In-Hospital vs Out-of Hospital) for the above clinical trials is summarized in **Table 3** on the following page.

Summary of Safety and Effectiveness

Potential
 Adverse Events
 Continued

Table 3
Major Adverse Clinical Events (In-Hospital vs Out-of-Hospital)

	TAXUS IV to 270 Days		TAXUS II to 365 Days		TAXUS I to 24 Months	
	TAXUS stent	Control Stent	TAXUS stent (n=131)	Control Stent (n=135)	TAXUS Stent (n=31)	Control Stent (n=30)
In-Hospital						
MACE	2.4% (16/662)	2.1%(14/652)	1.5% (2/131)	4.4% (6/136)	0.0% (0/31)	0.0% (0/30)
Death	0.0% (0/662)	0.3% (2/652)	0.0% (0/131)	0.7% (1/136)	0.0% (0/31)	0.0% (0/30)
Myocardial Infarction	2.4% (16/662)	2.1% (14/652)	1.5% (2/131)	3.7% (5/136)	0.0% (0/31)	0.0% (0/30)
Q-wave	0.2% (1/662)	0.2% (1/662)	0.0% (0/131)	0.7% (1/136)	0.0% (0/31)	0.0% (0/30)
Non Q-wave	2.3% (15/662)	2.0% (13/652)	1.5% (2/131)	2.9% (4/136)	0.0% (0/31)	0.0% (0/30)
Target Vessel Revascularization (TVR)	0.0%(0/662)	0.2% (1/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
Target Lesion Revascularization (TLR)	0.0%(0/662)	0.2%(1/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
TVR Remote	0.0%(0/662)	0.0%(0/652)	0.0% (0/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
TVR, CABG	0.0%(0/662)	0.0%(0/652)	0.0% (0/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
Stent Thrombosis	0.0%(0/662)	0.3%(2/652)	0.8% (1/131)	0.0% (0/136)	0.0% (0/31)	0.0% (0/30)
Out-of-Hospital						
MACE	6.2%(41/662)	13.0%(85/ 652)	9.2% (12/131)	17.8% (24/135)	3.2% (1/31)	10.0% (3/30)
Death	1.4%(9/662)	0.8%(5/652)	0.0% (0/131)	0.7% (1/135)	0.0% (0/31)	0.0% (0/30)
Myocardial Infarction	1.1% (7/662)	1.5%(10/652)	0.8% (1/131)	2.2% (3/135)	0.0% (0/31)	0.0% (0/30)
Q-wave	0.6%(4/662)	0.2%(1/652)	0.8% (1/131)	1.5% (2/135)	0.0% (0/31)	0.0% (0/30)
Non Q-wave	0.5%(3/662)	1.4%(9/652)	0.0% (0/131)	0.7% (1/135)	0.0% (0/31)	0.0% (0/30)
Target Vessel Revascularization (TVR)	4.7%(31/662)	11.8%(77/652)	9.2% (12/131)	15.6% (21/135)	3.2% (1/31)	10.0% (3/30)
Target Lesion Revascularization (TLR)	3.0%(20/662)	11.2%(73/652)	3.8% (5/131)	12.6% (17/135)	0.0% (0/31)	10.0% 3/30)
TVR Remote	1.7%(11/662)	1.1%(7/652)	3.1% (4/131)	3.0% (4/135)	3.2% (1/31)	0.0% (0/30)
TVR, CABG	0.5%(3/662)	0.3%(2/652)	3.1% (4/131)	0.7% (1/135)	0.0% (0/31)	3.3% (1/30)
Stent Thrombosis	0.6%(4/662)	0.5%(3/652)	0.8% (1/131)	0.0% (0/135)	0.0% (0/31)	0.0% (0/30)

MACE: Major Adverse Cardiac Events, comprised of Cardiac Death, MI and TVR.

TVR: Target Vessel Revascularization, defined as Ischemia-driven repeat percutaneous intervention of the target vessel or bypass surgery of the target vessel. A TVR will be considered as ischemia-driven if the target vessel diameter stenosis is $\geq 50\%$ by QCA and any of the following are present:

- the patient had a positive functional study corresponding to the area served by the target vessel;
- ischemic ECG changes at rest in a distribution consistent with the target vessel;
- ischemic symptoms referable to the target lesion.

Primary endpoint of TAXUS IV: 9-month TVR.

Summary of Safety and Effectiveness

**Potential
Adverse Events
Continued**

Adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries include but are not limited to:

- Abrupt stent closure
 - Acute myocardial infarction
 - Allergic reaction to anti-coagulant and/or antithrombotic therapy or contrast medium
 - Angina
 - Aneurysm
 - Arrhythmias, including ventricular fibrillation (VF) and ventricular tachycardia (VT)
 - Arteriovenous Fistula
 - Cardio Tamponade
 - Cardiogenic Shock
 - Death
 - Dissection
 - Emboli, distal (air, tissue or thrombotic emboli)
 - Emergent Coronary Artery Bypass Surgery (CABG)
 - Heart Failure
 - Hematoma
 - Hemorrhage, requiring transfusion
 - Hypotension/Hypertension
 - Infection
 - Infection and/or pain at the access site
 - Ischemia, myocardial
 - Perforation or Rupture
 - Pericardial effusion
 - Pseudoaneurysm, femoral
 - Renal Failure
 - Respiratory Failure
 - Restenosis of stented segment
 - Shock/Pulmonary edema
 - Spasm
 - Stent embolization
 - Stent thrombosis/occlusion
 - Stroke/cerebrovascular accident/TIA
 - Total occlusion of coronary artery
 - Vessel trauma requiring surgical repair or reintervention
-

Summary of Safety and Effectiveness

Potential Adverse Events Continued

Although systemic effects of paclitaxel are not anticipated, please refer to the Physicians' Desk Reference¹ for more information concerning potential adverse effects observed with paclitaxel.

Potential adverse events not captured above, that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug or stent coating
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

¹ Physicians' Desk Reference, published by Medical Economics Company, Inc. at Montvale, NJ.

Summary of Non Clinical Studies

Physical Testing Stent Material Specification Conformance

The following Stent Material Specification Conformance testing was performed on the coated stent (TAXUS Express stent), in accordance with the FDA Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices, May 1995, with any exceptions noted and justified. The testing conducted is listed in **Table 4**.

Table 4 Stent Material Specification and Conformance Testing		
Test Name	Test Purpose	Results
Corrosion Resistance	To assess the susceptibility of the TAXUS Express stent to corrosion.	Pass
Bare Stent Material Analysis	To determine the chemical composition of the raw stent material.	Pass
Surface Contamination	To detect evidence of surface contamination (FM) on the raw stent material.	Pass
Mechanical Properties: Tensile Strength and Elongation	To determine the tensile and elongation properties of the raw stent material.	Pass

Summary of Safety and Effectiveness

Summary of Non Clinical Studies Stent integrity testing on the TAXUS Express stent was conducted, as applicable, in accordance with the FDA Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology

Physical Testing Stent Integrity Devices, May 1995, with any exceptions noted and justified. The testing conducted is listed in **Table 5** below and continued on the next page.

Table 5		
Stent Integrity Testing		
Test Name	Test Purpose	Results
Finite Element Analysis (FEA)	To demonstrate the fatigue life on both the TAXUS Express stent, and the coating alone, using Finite Element Analysis.	Pass
Surface to Artery Ratio	To calculate the percentage of surface coverage of the stent relative to the stented vessel.	Pass
Stent Foreshortening	To determine the decrease in TAXUS Express stent length (stent foreshortening) when expanded to the stent's largest nominal diameter.	Pass
Stent Expansion Uniformity	To determine the uniformity of TAXUS Express stent expansion along the stent length following deployment, when the stent is expanded to its nominal diameter.	Pass
Stent Recoil	To quantify the amount of elastic recoil for the TAXUS Express stent after deployment.	Pass
Stent Flexibility/Conformability Testing	To determine the conformability (axial flexibility) of the stent in its expanded state by determining the pure bending moment of the stent.	Pass
Compression Resistance/Radial Hoop Strength	To determine the radial resistance of the TAXUS Express stent to external compression.	Pass
Stent Expansion/Safety Margin	To determine whether the deformation experienced by the stent undergoing expansion above the maximum rated diameter affects the coating integrity of the TAXUS Express stent.	Pass
Ten Year Accelerated Pulsatile Fatigue Testing	To assure that the TAXUS Express stent, when expanded to its largest intended diameters, will not show fatigue failure of the stent structure or coating, during a simulated 10-year time span.	Pass
Stent Radiopacity	To determine the radiopacity of the TAXUS Express stent relative to other currently marketed stents.	Pass

Summary of Safety and Effectiveness

Table 5, continued Stent Integrity Testing		
Test Name	Test Purpose	Results
Stent Particulate Testing	To determine the amount of particulate released from the catheter and stent during simulated delivery and deployment of the stent.	Pass
Magnetic Resonance Imaging (MRI)	Statement of acceptable use contained within the TAXUS Express DFU.	Pass
Stent Dimensional Verification	To verify the stent meets dimensional specifications.	Pass

Summary of Non Clinical Studies

Physical Testing Stent/Delivery System

Stent/Delivery System Testing on the TAXUS Express² Monorail and Over the Wire delivery systems was conducted in accordance with the Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices, May 1995, except where noted. The testing conducted is listed in **Table 6** below and continued on the following page.

Table 6 Stent/Delivery System Testing		
Test Name	Test Purpose	Results
Balloon in a Stent Burst, Balloon Bonds and Inflation Lumen Integrity Testing	To verify that the burst pressures meet the labeled Rated Burst Pressure specifications. Verification is also carried out to ensure that the inflation lumen and balloon bonds are capable of withstanding the Rated Burst Pressure.	Pass
Nominal Sizing Stent Distension and Compliance Labeling	To verify that the distention characteristics meet the specifications reflected on the labeling.	Pass
Stent Deployment	To determine the pressure required to fully deploy the stent.	Pass
Repeat Balloon Inflation	To verify that the delivery systems are capable of withstanding repeated inflation to Rated Burst Pressure within the stent.	Pass
System/Stent and Balloon Crossing Profile	To determine the pre-deployed profile of the delivery system for each stent diameter.	Pass
Stent Securement Force Testing	To assess the force required to dislodge a crimped stent from its catheter.	Pass
Balloon Inflation/Deflation Testing	To assure the inflation and deflation times for the delivery systems meet specification.	Pass

Summary of Safety and Effectiveness

Table 6, continued		
Stent/Delivery System Testing		
Test Name	Test Purpose	Results
Shaft Diameters	To assure the proximal shaft, distal shaft and distal tip diameters for the delivery systems meet specification.	Pass
Pre-and Post-Deployment Catheter Withdrawal Into a Guide	To verify that the delivery systems can be safely withdrawn back into the recommended guide catheter sizes both before, and after, stent deployment.	Pass
System Track Testing	To assure that the tracking force of the delivery systems through a simulated artery is comparable to currently marketed devices.	Pass
Full Unit Tensile Testing	To assure the tensile strength of the delivery systems meet specifications.	Pass
Post Track Stent Securement Force	To assess the force required to dislodge a crimped stent from its catheter after it has been tracked through a simulated tortuous artery model.	Pass
Non-Coaxial Withdrawal into a Guide Catheter	To determine the ability of the TAXUS Express ² product to be safely withdrawn into the guide catheter when the entry is non-coaxial.	Pass

Summary of Non Clinical Studies

Chemistry Studies

Testing on the TAXUS Express² Monorail and Over the Wire delivery systems was conducted using the United States Pharmacopeia or International Conference on Harmonization (ICH) Guidelines as a guide, where applicable. The Chemistry studies conducted are listed in **Table 7** on the following page.

Summary of Safety and Effectiveness

Table 7 Chemistry Studies		
Test Name	Test Purpose	Results
Paclitaxel Identity, Content Assay, Degradants	To verify the drug in the stent coating is paclitaxel and that the drug content of stents and drug degradation products meet specifications and label claim	Pass
Kinetic Drug Release	To verify that the release of paclitaxel from the coated stent over time meets specifications	Pass
Drug Content Uniformity	To verify that the drug content of each coated stent from the same batch meets specifications.	Pass
Residual Solvents	To verify that residual levels of the solvents used in the manufacturing process are at acceptable levels	Pass
Content Uniformity Along the Length of the Stent	To evaluate the uniform distribution of drug along the length of the stent	Uniformity Acceptable
Animal and Clinical Systemic Paclitaxel Levels	To assess systemic levels of paclitaxel after implantation of TAXUS stents in animal models and in early Clinical trials (TAXUS I and II)	None detected
Pharmacokinetics	No standard pharmacokinetics study to determine t_{max} , C_{max} , $t_{1/2}$, AUC, CL was conducted given the results of testing for systemic levels of paclitaxel noted above	N/A
Tissue Distribution	To measure the in vivo levels of paclitaxel in vascular tissue local to the implant site and in various organs after implantation of TAXUS stents in animals	Levels measured
In vitro-In vivo Correlation	To develop an in vitro method to measure drug release from the TAXUS stent which will demonstrate a close correlation with release detected in vivo	Correlation shown
Translute Biostability	To assess the stability of the polymer carrier after implantation of TAXUS stents through molecular weight measurements	Pass
Coating Integrity	To examine the integrity of the coating on the TAXUS stent after long-term implantation in animals	Pass

Summary of Safety and Effectiveness

Summary of Non Clinical Studies

Device Biocompatibility

A series of biocompatibility tests were conducted to demonstrate the components of the TAXUS Express² Paclitaxel-Eluting Coronary Stent System (Monorail and Over-the-Wire) are non-toxic. Testing was conducted in accordance with the FDA Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices, May 1995. Additionally, testing was conducted in accordance with the International Standard EN/ISO-10993, “Biological Evaluation of Medical Devices Part 1:-Evaluation and Testing”. The testing is summarized in **Table 8**.

Table 8 Stent and Delivery System Biocompatibility Test Results		
Test Name	Test Purpose	Results
Cytotoxicity MEM Elution	Evaluate Biocompatibility	Non-cytotoxic
Skin Sensitization Kligman	Evaluate Biocompatibility	Non-skin sensitizing
Intracutaneous Injection	Evaluate Biocompatibility	Met USP Injection Test
Systemic Toxicity	Evaluate Biocompatibility	Not a systemic toxin
Material Mediated Rabbit Pyrogenicity	Evaluate Biocompatibility	Non-pyrogenic
Pyrogenicity, LAL	Evaluate Biocompatibility	Non-pyrogenic
Subchronic Toxicity	Evaluate Biocompatibility	No subchronic toxicity
Hemolysis	Evaluate Biocompatibility	Non-hemolytic
<i>In-Vitro</i> Hemocom- patibility Assay	Evaluate Biocompatibility	Pass
Thrombogenicity, Lee and White Coagulation	Evaluate Biocompatibility	Pass
USP Physicochemical Test for Plastics	Evaluate Biocompatibility	Pass
Intramuscular Implant-14 days	Evaluate Biocompatibility	Non-toxic
Intramuscular Implant- 30 Days	Evaluate Biocompatibility	Non-toxic

Summary of Safety and Effectiveness

Summary of Non Clinical Studies

Translute Biocompatibility and Vascular Compatibility

Tests were conducted to support the biocompatibility of the Translute polymer on stainless steel coupons or cast films using ISO 10993 biocompatibility recommendations for a permanent implant. In addition, vascular compatibility testing was carried out on Translute coated stents or grafts (without paclitaxel) in porcine and canine models. Neointimal thickness, healing, endothelial-cell coverage (28, 80, and 180 days on stents in swine), patency, graft migration, polymer biodegradation, and carcinogenicity (6, 12, and 24 months on grafts in canines) were assessed. In all studies the Translute was safe, non-toxic and non-pyrogenic, healing was complete, and no evidence was found for polymer degradation, or for precancerous or cancerous changes in adjacent vascular walls. The testing is summarized in **Table 9** below and **Table 10** on the following page.

Table 9 Translute Biocompatibility/Vascular Compatibility Test Summary		
Test Name	Test Purpose	Conclusions
Cytotoxicity, MEM Elution	Evaluate Biocompatibility	Non-cytotoxic
Skin Sensitization Kligman	Evaluate Biocompatibility	Non-skin sensitizing
Intracutaneous Injection	Evaluate Biocompatibility	Met USP Injection Test requirements
Systemic Toxicity	Evaluate Biocompatibility	Not a systemic toxin
Material Mediated Rabbit Pyrogenicity	Evaluate Biocompatibility	Non-pyrogenic
Mutagenicity Studies		
Bacterial Reverse Mutation assay (Ames Test)	Evaluate Biocompatibility	Non-Mutagenic
<i>In Vivo</i> micronucleus test in mice	Evaluate Biocompatibility	Non- Mutagenic
<i>In Vitro</i> chromosomal Aberrations in Human Blood Lymphocytes	Evaluate Biocompatibility	Non- Clastogenic

Summary of Safety and Effectiveness

Table 10		
Translute Biocompatibility/Vascular Compatibility Test Summary, continued		
Test Name	Test Purpose	Conclusion
Implantation Studies		
Chronic Toxicity in Mice	Evaluate Biocompatibility	No chronic systemic toxicity.
Porcine Studies	Evaluate Biocompatibility and Vascular Compatibility	Findings support vascular compatibility and biocompatibility.
Canine studies	Evaluate Biocompatibility and Vascular Compatibility	Results support vascular biocompatibility and long-term biostability of Translute polymer. No evidence of precancerous or cancerous change in adjacent vascular wall. Two-year grafts widely patent, well endothelialized, with stable neointima. No evidence of biodegradation of the Translute polymer in any of the grafts
Hemocompatibility		
Direct Hemolysis – Rabbit Blood	Evaluate Biocompatibility	Non Hemolytic
Thrombogenicity	Evaluate Biocompatibility	Non-thrombogenic
Styrene Assay		
Styrene Monomer Residual Assay by Gas Chromatography (Flame Ionization Detector)	Determine the ability to leach styrene monomer from Translute polymer under physiologically relevant conditions.	No styrene monomer detected

Summary of Safety and Effectiveness

Summary of Non Clinical Studies

Preclinical data for the drug eluting stent indicates no adverse coronary arterial effects, downstream myocardial changes or systemic adverse events, thus establishing vascular compatibility and product safety.

Paclitaxel

Biocompatibility

Table 11 summarizes findings from additional studies conducted to determine paclitaxel's local toxicity profile in cell types and concentrations relevant to the treatment of restenosis.

Table 11		
Paclitaxel Biocompatibility Test Summary		
Test Name	Test Purpose	Conclusion(s)
Assessment of One Year Porcine Coronary Implants for Pre-neoplastic Change Summary	Histopathological evaluation for pre-neoplastic or neoplastic changes.	Unlikely carcinogenic risk.
Bacterial Mutagenicity (Ames Assay)	Determination of mutagenic potential of paclitaxel.	Non-genotoxic.
In vivo Mouse Micronucleus Test	Determination of the ability of paclitaxel to form micronuclei in immature polychromatic erythrocytes (PCE) present in the bone marrow of CD-1 mice.	Non-genotoxic.
Chromosomal Aberrations in Chinese Hamster Ovary (CHO) cells and human lymphocytes	Determination of chromosomal aberrations in CHO cells and human lymphocytes.	Non-genotoxic.
In vitro Thrombogenicity Study Summary	Comparison of flow rate, visual inspection of thrombus, and thrombus mass at the end of the study.	Non-thrombogenic.
Effects of Paclitaxel on Human Smooth Muscle Cells Study Summary	Determination of cytotoxicity potential of paclitaxel.	Non-cytotoxic.
Effects of Paclitaxel on DNA and Apoptosis in Human Smooth Muscle Cells Study Summary	Determine effect of paclitaxel on DNA damage and cell apoptosis of human coronary artery smooth muscle cell (hSMC).	No DNA fragmentation. Not associated with apoptosis in hSMC.

Summary of Safety and Effectiveness

Summary of Non Clinical Studies

GLP Studies

Three studies evaluated the safety of the TAXUS stent in a porcine model: a 360-day controlled study of 3 dose-densities of a moderate-release formulation of paclitaxel; a 180-day study of the safety of overlapping stent segments of a moderate-release formulation of paclitaxel; and a 180-day study of concomitant use of ticlopidine with a slow-release formulation of paclitaxel. Paclitaxel-eluting stents demonstrated excellent safety, no stent-related mortality, satisfactory endothelialization, and no gross thrombus. The intended effect of paclitaxel, a reduction in smooth muscle histologic indices of restenosis, was observed without positive remodeling or reduction of neointimal or endothelial cell coverage. Concomitant use of ticlopidine did not affect safety. Results of testing have consistently demonstrated safety and excellent healing in higher dose-densities, and in faster release formulations, than the product to be marketed for human use.

Animal Testing

Feasibility Studies

Feasibility studies were conducted using various dose-densities and release formulations of paclitaxel, on both NIR™ and Express stents. These studies served as a basis for dose and release-formulation selection for clinical investigations.

Summary of Clinical Studies

TAXUS IV (US Pivotal)

In suitable patients, elective TAXUS™ Express™ Paclitaxel-Eluting stent placement in native coronary *de novo* lesions resulted in significantly lower rates of target vessel revascularization (TVR) (4.7% vs 12.0%, difference [95% CI]; -7.3% [-10.2%, -4.3%]), target lesion revascularization (TLR) (3.0% vs 11.3%, difference [95% CI]; -8.3% [-11.1%, -5.6%]), and MACE (8.5% vs 15.0%, difference [95% CI]; -6.6% [-10.0%, -3.1%]) as compared to controls. In the TAXUS Express treatment group 9-month angiography revealed: binary restenosis (>50% diameter stenosis) in both the stented segment (5.5% vs 24.4%, difference [95% CI]; -18.9% [-24.7%, -13.1%]) and analysis segment (stented area \pm 5 mm proximal and distal) (7.9% vs 26.6%, difference [95% CI]; -18.7% [-24.8%, -12.5%]), and in-stent late loss (0.39 mm vs 0.92 mm difference, [95% CI]; -0.53 [-0.62, -0.44]) were significantly reduced as compared to control. There was no evidence of edge effect \pm 5 mm proximal or distal to the stent. In the TAXUS Express group there was significantly lower percent in-stent net volume obstruction as determined by intravascular ultrasound (IVUS) (12.2% vs 29.4%, difference [95% CI]; -17.19% [-21.29, -13.10]) at 9 month follow-up as compared to control.

Reference **Table 12** for a summary of the Principle Safety and Effectiveness Results for TAXUS IV.

Summary of Safety and Effectiveness

Summary of Clinical Studies

TAXUS II (International Efficacy Study)

In suitable patients, elective TAXUS™ NIRx™ Paclitaxel-Eluting stent placement using the slow release formulation in native coronary *de novo* lesions resulted in significantly lower percent in-stent net volume obstruction as determined by intravascular ultrasound (IVUS) (7.91% vs 23.90%, difference [95% CI]; -15.18% [-18.92, -11.43]) at 6 month follow-up as compared to the uncoated NIR™ control stent. The TAXUS NIRx (SR) treatment group exhibited significantly lower major adverse cardiac event (MACE) rates at 12 months follow-up (10.9% vs 22.0%, difference [95% CI]; -11.1% [-20.0%, -2.2%]) as compared to controls. In the TAXUS NIRx (SR) treatment group 6-month angiography revealed: binary restenosis (>50% diameter stenosis) in both the stented segment (2.3% vs 17.9%, difference [95% CI]; -15.6% [-22.6%, -8.6%]) and analysis segment (stented area ± 5 mm proximal and distal) (5.5% vs 20.1%, difference [95% CI]; -14.7% [-22.5%, -6.8%]), and in-stent late loss (0.31 mm vs 0.79 mm difference, [95% CI]; -0.48 [-0.58, -0.38]) were significantly reduced. There was no evidence of edge effect ± 5 mm proximal or distal to the stent. There was a significant reduction in the incidence of target lesion revascularization (TLR) at 12 months (4.7% vs 12.9%, difference [95% CI]; -8.2% [-15.0%, -1.5%]) in the TAXUS NIRx (SR) arm as compared to control.

Reference **Table 13** for a summary of the Principle Safety and Effectiveness Results for TAXUS II.

Summary of Clinical Studies

TAXUS I (Randomized Feasibility)

In suitable patients, elective TAXUS™ NIRx™ Paclitaxel-Eluting stent placement using the slow release formulation in native coronary *de novo* lesions resulted in significantly lower percent diameter stenosis (%DS) at 6 months (13.56% vs 27.23%, $p < 0.001$) as compared to control receiving an uncoated NIR™ stent. At 6-months Minimum Lumen Diameter (MLD) was significantly greater (2.60 mm vs 2.16 mm, $p = 0.007$) and late loss significantly reduced (0.36 mm vs 0.71 mm, $p = 0.007$) in the TAXUS NIRx (SR) treatment group. Binary restenosis (diameter stenosis >50%) was 0% in the TAXUS arm vs 10% in the control arm at 6 months. The overall MACE rate at 24 months was 3% (1/31 patients) for the TAXUS NIRx (SR) arm as compared to 10% (3/30 patients) in the control arm. The event in the TAXUS NIRx (SR) arm was due to a target vessel revascularization (TVR) that occurred between 6 and 12 month follow-up.

Reference **Table 14** for a summary of the Principle Safety and Effectiveness Results for TAXUS I.

Summary of Safety and Effectiveness

Table 12 TAXUS IV Principal Safety and Effectiveness Results					
	TAXUS (SR) (N=662)	Control (N=652)	Relative Risk [95% CI]	Difference [95% CI]	P Value
Effectiveness Measures					
Clinical Procedural Success	97.3% (643/661)	97.4% (635/652)	1.00 [0.98, 1.02]	-0.1% [-1.9%, 1.6%]	1.000
Technical Success	97.9% (648/ 662)	98.2% (640/ 652)	1.00 [0.98, 1.01]	-0.3% [-1.8%, 1.2%]	0.844
9-month Target Vessel Revascularization	4.7% (31/ 662)	12.0% (78/ 652)	0.39 [0.26, 0.59]	-7.3% [-10.2%, -4.3%]	<0.001
9-month In-stent restenosis	5.5% (16/ 291)	24.4% (65/ 266)	0.23 [0.13, 0.38]	-18.9% [-24.7%,-13.1%]	<0.001
9-month Analysis segment restenosis	7.9% (23/ 291)	26.6% (71/ 267)	0.30 [0.19, 0.46]	-18.7% [-24.8%,-12.5%]	<0.001
MLD (mm), In-Stent					
Post-Procedure	2.65 +/- 0.42 (373) (1.53 , 3.92)	2.67 +/- 0.41 (351) (1.67 , 3.76)	NA	-0.01 [-0.07,0.05]	0.658
9-Month	2.26 +/- 0.58 (291) (0.00,3.88)	1.75 +/- 0.65 (266) (0.00,3.36)	NA	0.51 [0.41,0.61]	<0.001
MLD (mm), Analysis Segment					
Post Procedure	2.26 +/- 0.48 (374) (1.28,3.66)	2.29 +/- 0.50 (356) (1.01,3.62)	NA	-0.03 [-0.10,0.04]	0.456
9-Month	2.03 +/- 0.55 (291) (0.00,3.32)	1.68 +/- 0.61 (267) (0.00,3.15)	NA	0.35 [0.26, 0.45]	<0.001
Diameter Stenosis, In-Stent (%)					
Post Procedure	4.21 +/- 10.84 (373) (-35.16,31.35)	5.16 +/- 11.41 (351) (-54.40,40.86)	NA	-0.95 [-2.57, 0.67]	0.250
9-Month	17.43 +/-17.71 (291) (-27.83,100.00)	37.24 +/- 19.76 (266) (-7.61,100.00)	NA	-19.82 [-22.93,16.70]	<0.001
Diameter Stenosis, Analysis Segment (%)					
Post Procedure	19.16 +/- 9.67 (374) (-12.48,49.61)	19.33 +/- 10.45 (356) (-3.64,59.27)	NA	-0.17 [-1.63, 1.29]	0.822
9-Month	26.29 +/- 15.45 (291) (0.36,100.00)	39.79 +/- 18.45 (267) (4.13,100.00)	NA	-13.50 [-16.31,-10.68]	<0.001
Late Loss, In-Stent (mm)	0.39 +/- 0.50 (291) (-0.85 , 2.68)	0.92 +/- 0.58 (266) (-0.95 , 2.84)	NA	-0.53 [-0.62, -0.44]	<0.001
Late Loss, Analysis Segment (mm)	0.23 +/- 0.44 (291) (-0.69 , 2.68)	0.61 +/- 0.57 (267) (-0.56 , 2.75)	NA	-0.38 [-0.47, -0.30]	<0.001
9-Month % Net Volume Obstruction	12.20 +/- 12.44 (81) (0.00 , 53.96)	29.40 +/- 14.05 (80) (0.00 , 64.46)	NA	-17.19 [-21.29,-13.10]	<0.001

Summary of Safety and Effectiveness

Table 12, continued
TAXUS IV Principal Safety and Effectiveness Results

	TAXUS (SR) (N=662)	Control (N=652)	Relative Risk [95% CI]	Difference [95% CI]	P Value
Safety Measures					
In-hospital MACE	2.4% (16/662)	2.1% (14/652)	1.13 [0.55, 2.29]	0.3% [-1.3%, 1.9%]	0.854
Out-of-Hospital MACE to 9-months	6.2% (41/662)	13.0% (85/652)	0.48 [0.33, 0.68]	-6.8% [-10.0%, -3.7%]	<0.001
MACE to 9-months	8.5% (56/662)	15.0% (98/652)	0.56 [0.41, 0.77]	-6.6% [-10.0%, -3.1%]	<0.001
TVR to 9-months (Primary Endpoint)	4.7% (31/662)	12.0% (78/652)	0.39 [0.26, 0.59]	-7.3% [-10.2%, -4.3%]	<0.001
Stent Thrombosis (to 30 days)	0.3% (2/662)	0.3% (2/652)	0.98 [0.14, 6.97]	-0.0% [-0.6%, 0.6%]	1.000
Stent Thrombosis (to 9 months)	0.6% (4/662)	0.8% (5/652)	0.79 [0.21, 2.92]	-0.2% [-1.1%, 0.7%]	0.751
CVA to 9 months	1.5% (10/662)	0.8% (5/652)	1.97 [0.68, 5.73]	0.7% [-0.4%, 1.9%]	0.299
Serious Bleeding Complications	2.6% (17/662)	1.8% (12/652)	1.40 [0.67, 2.90]	0.7% [-0.9%, 2.3%]	0.454
Serious Vascular Complications	1.5% (10/662)	1.8% (12/652)	0.82 [0.36, 1.89]	-0.3% [-1.7%, 1.1%]	0.673
Platelet Disorders	0.6% (4/662)	0.8% (5/652)	0.79 [0.21, 2.92]	-0.2% [-1.1%, 0.7%]	0.751
Hematological Dyscrasia to 9 months	1.5% (10/662)	0.5% (3/652)	3.28 [0.91, 11.9]	1.1% [-0.0%, 2.1%]	0.091

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.

Difference = TAXUS SR – Control. Relative Risk (RR) = TAXUS SR / Control. SE of RR = $\sqrt{\{(1-p_1)/n_{11} + (1-p_2)/n_{21}\}}$.

SE of Difference = $\sqrt{(p_1q_1/n_1 + p_2q_2/n_2)}$ for proportions, = $\sqrt{[(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\} / (N-2)]}$ for continuous variables.

95% CI of Difference = Diff±1.96·SE. 95% CI of RR = RR·exp(±1.96·SE).

P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.

Undef = Undefined.

All event data were adjudicated by the independent Clinical Events Committee (CEC). All QCA data were assessed by the Angiographic Core Laboratory. All IVUS data were assessed by the IVUS Core Laboratory.

Primary endpoint is 9-month TVR.

Clinical Procedural Success: using the assigned study device to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.

Technical success: successful delivery and deployment of the study stent to the target lesion, without balloon rupture, embolization, or use of a device outside the treatment strategy.

MLD = Minimum Lumen Diameter

9-Month MACE: the proportion of patients who experience a MACE up to the 9-month follow-up. MACE includes cardiac death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).

30-Day MACE: binary MACE rate to 30 days post-procedure.

9-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 9-month follow-up.

The Analysis Segment consists of the proximal edge, stent, and the distal edge, where each edge segment contains up to 5mm immediately outside the stent.

Serious Bleeding Complications included: hemorrhage (gastric ulcer, mediastinal, rectal, upper GI, and GI not specified), hematuria, hemoptysis, and hemothorax. Serious Vascular Complications included: hematoma (catheter site and not specified), hemorrhage (catheter site and retroperitoneal), arterial injury, and vascular pseudoaneurysm. Platelet disorders included thrombocytopenia. Hematologic dyscrasia included: anemia, and pancytopenia.

Summary of Safety and Effectiveness

Table 13
TAXUS II Principal Safety and Effectiveness Results

	TAXUS II (SR) (N=131)	Control (N=136)	Relative Risk [95% CI]	Difference [95% CI]	P Value
Effectiveness Measures					
Clinical Procedural Success	95.4% (125/131)	93.4% (127/136)	1.02 [0.96, 1.08]	2.0% [-3.5%, 7.5%]	0.5976
Technical Success	97.7% (128/131)	98.5% (134/136)	0.99 [0.96, 1.03]	-0.8% [-4.1%, 2.4%]	0.6794
6-Month % Net Volume Obstruction	7.85±9.87 (118) (-0.05, 47.95)	23.17±18.19 (125) (-0.00, 77.07)	NA	-15.32 [-19.03, -11.61]	<0.0001
6-month In-stent restenosis	2.3% (3/128)	17.9% (24/134)	0.13 [0.04, 0.42]	-15.6% [-22.6%, -8.6%]	<0.0001
6-month Analysis segment restenosis	5.5% (7/128)	20.1% (27/134)	0.27 [0.12, 0.60]	-14.7% [-22.5%, -6.8%]	0.0004
MLD (mm), Stented Segment					
Post-Procedure	2.53±0.29 (128) (1.77, 3.19)	2.58±0.37 (135) (1.73, 3.57)	NA	-0.05 [-0.13, 0.03]	0.2132
6-Month	2.23±0.47 (128) (0.00, 3.39)	1.79±0.54 (134) (0.51, 3.02)	NA	0.44 [0.32, 0.56]	<0.0001
MLD (mm), Analysis Segment					
Post Procedure	2.15±0.37 (128) (1.10, 2.99)	2.23±0.43 (135) (1.27, 3.26)	NA	-0.08 [-0.17, 0.02]	0.1202
6-Month	2.01±0.46 (128) (0.00, 3.18)	1.70±0.49 (134) (0.51, 3.02)	NA	0.31 [0.20, 0.43]	<0.0001
Diameter Stenosis, Stented Segment (%)					
Post Procedure	10.90±6.52 (128) (-5.00, 29.00)	10.20±5.94 (135) (-6.00, 25.00)	NA	0.70 [-0.81, 2.20]	0.3659
6-Month	19.53±12.71 (128) (-3.00, 100.00)	31.77±17.11 (134) (-9.00, 79.00)	NA	-12.25 [-15.91, -8.59]	<0.0001
Diameter Stenosis (%), Analysis Segment					
Post Procedure	23.07±9.27 (128) (7.50, 54.50)	21.24±8.41 (135) (5.00, 52.00)	NA	1.83 [-0.31, 3.97]	0.0943
6-Month	26.79±12.78 (128) (5.00, 100.00)	35.11±15.09 (134) (7.00, 79.00)	NA	-8.32 [-11.71, -4.93]	<0.0001
6-Month Late Loss (mm), Stented Segment	0.31±0.38 (127) (-0.54, 2.20)	0.79±0.45 (134) (-0.11, 2.09)	NA	-0.48 [-0.58, -0.38]	<0.0001
Safety Measures					
30-Day MACE	2.3% (3/131)	4.4% (6/136)	0.52 [0.13, 2.03]	-2.1% [-6.4%, 2.2%]	0.5010
6-Month MACE	8.5% (11/130)	19.5% (26/133)	0.43 [0.22, 0.84]	-11.1% [-19.4%, -2.8%]	0.0125
12-Month MACE	10.9% (14/129)	22.0% (29/132)	0.49 [0.27, 0.89]	-11.1% [-20.0%, -2.2%]	0.0191
TLR Free to 365 days	95.4%	87.4%	1.09 [1.01, 1.18]	8.0% [1.3%, 14.7%]	0.020
Stent Thrombosis ≤ 1 Day	0.8% (1/131)	0.0% (0/136)	Undef [Undef, Undef]	0.8% [-0.7%, 2.3%]	0.4906
Stent Thrombosis ≤ 365 Days	1.5% (2/131)	0.0% (0/136)	Undef [Undef, Undef]	1.5% [-0.6%, 3.6%]	0.2398

Numbers are % (Count/Sample Size) or Mean±SD (N) (Min, Max). CI = Confidence Interval.

Difference = TAXUS SR – Control. Relative Risk (RR) = TAXUS SR / Control. SE of RR = $\sqrt{\{(1-p_1)/n_{11} + (1-p_2)/n_{21}\}}$.

SE of Difference = $\sqrt{(p_1q_1/n_1 + p_2q_2/n_2)}$ for proportions, = $\sqrt{[(1/n_1 + 1/n_2)\{(n_1-1)s_1^2 + (n_2-1)s_2^2\}/(N-2)]}$ for continuous variables.

95% CI of Difference = Diff±1.96·SE. 95% CI of RR = RR·exp(±1.96·SE).

P-values are two-sided and from Student's t test for continuous variables and Fisher's exact test for discrete variables.

Undef = Undefined.

Primary endpoint is 6-Month Percent Stented Segment Net Volume Obstruction, determined by IVUS.

Event/success rates are number of patients with the outcome ÷ the number of patients evaluable for the outcome.

Clinical Procedural Success: using the assigned study device to achieve an in-target-lesion diameter stenosis <30% in the average of 2 near-orthogonal projections, as visually assessed by the physician, without the occurrence of in-hospital MACE.

6-Month MACE: the proportion of patients who experience a MACE up to the 6-month follow-up. MACE includes death, myocardial infarction (MI) including Q- and non-Q-wave MI, and target vessel revascularization (TVR).

30-Day MACE: binary MACE rate to 30 days post-procedure.

12-Month MACE: binary MACE rate to 365 days post-procedure.

6-Month Restenosis: the proportion of patients who demonstrate ≥50% diameter stenosis of the target lesion by Quantitative Coronary Analysis (QCA) performed at the Angiographic Core Laboratory at the 6-month follow-up.

The Analysis Segment consists of the proximal edge, stent, and the distal edge, where each edge segment contains up to 5mm immediately outside the stent.

Summary of Safety and Effectiveness

Table 14 TAXUS I Effectiveness and Safety Results			
Safety Measures and Other Clinical Events	TAXUS NIRx™ (SR) N=31	NIR™ Control N=30	<i>p-value</i>
MACE (30-day)	0% (0/31)	0% (0/30)	NA
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	0% (0/31)	0% (0/30)	NA
MACE (12-Month)	3% (1/31)	10% (3/30)	0.612
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	3% (1/31)	10% (3/30)	0.612
MACE (2-Year)	3% (1/31)	10% (3/30)	0.612
Cardiac Death	0% (0/31)	0% (0/30)	NA
Q-Wave MI	0% (0/31)	0% (0/30)	NA
TVR (CABG and/or PCI)	3% (1/31)	10% (3/30)	0.612
Stent Thrombosis to 2 years	0% (0/31)	0% (0/31)	NA
QCA In-Stent Lesion Characteristics			
Pre-procedure			
RVD, mm	2.99±0.46 (31)	2.94±0.52 (29)	0.699
MLD, mm	1.30±0.43 (31)	1.23±0.43 (29)	0.558
%DS	56.51±12.26 (31)	57.82±13.24 (29)	0.692
Lesion length, mm	10.70±3.27 (31)	11.89±4.93 (29)	0.272
Post-procedure			
MLD, mm			0.414
%DS	6.12±9.49 (31)	2.95±0.34 (31)	0.096
6-Month follow-up			
RVD, mm	3.02±0.47 (30)	3.01±0.53 (29)	0.899
MLD, mm	2.60±0.49 (30)	2.19±0.65 (29)	0.008
%DS	13.56±11.77 (30)	27.23±16.69 (29)	<0.001
Restenosis Rate ≥50%	0% (0/30)	10% (3/29)	0.112
Late lumen loss, mm	0.36±0.48 (30)	0.71±0.47 (26)	0.009
Loss index	0.22±0.29 (30)	0.45±0.29 (26)	0.004

Conclusions from Clinical and Non Clinical Studies

Based on the non-clinical and clinical studies presented in this section, it is reasonable to conclude that the benefits of this device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the instructions for use.